REMARKS

Claims 74-76 and 79-98 were pending in the application. Claims 74 and 95 have been amended and claims 77-85 and 87-93 have been cancelled. New claims 99 and 100 have been added. Accordingly, after the amendments presented herein have been entered, claims 74-76, 86, and 94-100 will remain pending.

Support for the amendments to the claims and the new claims can be found throughout the specification and claims as originally filed. Specifically, support for the amendment to claim 95 can be found at, for example, page 14, lines 1-34 of the specification. Support for new claims 99 and 100 can be found in Example 9, and at, for example, page 7, lines 13-15 of the specification.

No new matter has been added. The foregoing claim amendments and cancellations of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and were done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Improper Withdrawal of Claims 79-97

The Examiner has indicated that claims 79-97 are withdrawn as "being directed to subject matter that was not elected in the response to Restriction Requirement mailed January 14, 2004." The Examiner states that "Applicant has copied the subject matter from cancelled, non-elected claims 1-73 and incorporated them as dependent claims in the elected invention."

Applicants respectfully submit that the withdrawal of claims 79-97 is improper for the following reasons. Applicants elected Group V directed to methods of preparing a therapeutic agent in the Response to Restriction Requirement filed on February 17, 2004. Claim 74 is directed to a method of preparing a therapeutic agent having the structure I-L-P'. Withdrawn claims 79-97 depend from and further limit claim 74, *i.e.*, further define the identity of I, L, and P' in the therapeutic agent prepared by the method of claim 74. Therefore, the withdrawn claims are not directed to non-elected subject matter but, rather, are directed to methods of preparing a therapeutic agent having the I-L-P' structure as elected in the Response to Restriction Requirement.

Accordingly, Applicants respectfully request that the Examiner reconsider and reverse the withdrawal of claims 79-97.

Rejection of Claims 74-76 Under of 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 74-76 under 35 U.S.C. § 112, first paragraph because the specification, "while being enabling for a method for preparing Aβ(16-30)-hFc, does not reasonably provide enablement for preparing any therapeutic agents, any as of yet unspecified peptide-target protein combinations, or any agents containing D-amino acid." The Examiner states

> [t]he claims as instantly presented represent an invitation to experiment where one would discover a therapeutic agents represented by the formula I-L-P'. While therapeutic agents represented by the formula I-L-P' may constitute a fecund ground for investigation, the CAFC ruled in *Genentech Inc. v. Novo NordiskA/S* (CA FC) **42 USPQ2d 1001** (1997) that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Citing *Brenner* v. *Manson*, **383 U.S. 519, 536, 148 USPQ 689, 696** (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). Therefore the CAFC stated that tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. That requirement has not been met in the instant specification with respect to the any therapeutic agents represented by the formula I-L-P' which in turns has any therapeutic activity for any given disease, disorder, or injury save for AP(16-30)-hFc.

Applicants traverse this rejection for the following reasons.

Applicants believe that the claims are fully enabled by the specification as filed for the reasons of record. However, in the interest of expediting prosecution, and in no way acquiescing to the validity of the Examiner's rejection, Applicants have amended the claims to be directed to methods of preparing therapeutic agents comprising the formula I-L-P', wherein I is an immunoglobulin heavy chain constant region or fragment thereof that retains the ability to bind an Fc receptor; L is a linker group or a direct bond and P' is ***a peptide capable of binding to a β-amyloid protein***. By amending the claims so that P' is a peptide capable of binding to a β-amyloid protein, the claims are limited to methods for preparing a therapeutic agent that has a single function, *i.e.*, binds a β-amyloid protein. Therefore, the claims do not cover the

preparation of an agent that has "any therapeutic activity for any given disease, disorder or injury" as asserted by the Examiner.

For the reasons of record, Applicants submit that the I and L components of the therapeutic agents are fully enabled by the specification as filed. Further, Applicants' specification provides detailed teachings regarding P' wherein P' is a peptide capable of binding a β–amyloid protein. Applicants teach specific fragments of the β-amyloid peptide (β-AP) that one of skill in the art would use to prepare the therapeutic agents of the invention. For example, Applicants teach that P' is designed based upon the amino acid sequence of the natural β-amyloid peptide (see page 13, lines 34-35 of the specification). Then, Applicants proceed with a detailed description of how the skilled artisan would design and prepare the claimed compounds having a P' component that binds a β-amyloid protein (see, for example, pages 14-23 of the specification). Applicants further teach that, in a preferred embodiment, P' is designed based upon the amino acid sequence of the Aβ aggregation core domain (see, for example, page 14, lines 13-15 of the specification) and also describe specific peptide fragments of β-AP, *e.g.*, fragments comprising $A\beta_{16-30}$, $A\beta_{17-20}$, $A\beta_{17-21}$, $A\beta_{16-25}$, $A\beta_{1-25}$, $A\beta_{1-40}$, and $A\beta_{1-42}$, that may be used in the I-L-P' compounds of the invention (see, for example, page 14, lines 32-35 and page 45, lines 12-16 of the specification).

Applicants further provide working examples describing the generation and testing of various I-L-P' compounds containing a P' component that binds a β-amyloid peptide. For example, Example 5 describes experiments with compounds in which the Fc region of mouse IgG was fused to amino acid residues 1-40, 1-42, 10-25, 16-30, 17-21 or 17-21 (A21L) of the β-AP. Applicants also present *in vitro* and *in vivo* data demonstrating the efficacy of the generated compounds. For instance, Applicants present data indicating that a Aβ(16-30)-hFc is capable of significantly decreasing plaque burden at the site of administration in mice transgenic for the Swedish mutation.

In *Wands*, the court reversed the rejection for lack of enablement under 35 U.S.C. 112, first paragraph, concluding that undue experimentation would not be required to practice the invention. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). The rationale behind this decision was that

> [t]he nature of monoclonal antibody technology is such that experiments first involve the entire attempt to make monoclonal hybridomas to determine which

> ones secrete antibody with the desired characteristics. The court found that the specification provided considerable direction and guidance on how to practice the claimed invention and presented working examples, that all of the methods needed to practice the inventions were well known, and that there was a high level of skill in the art at the time the application was filed. Furthermore, the applicant carried out the entire procedure for making a monoclonal antibody against HBsAg three times and each time was successful in producing at least one antibody which fell within the scope of the claims. See MPEP § 2164.06(b).

Similarly, in the present case, Applicants submit that the level of skill in the art of making fusion proteins comprising immunoglobulin heavy chain constant regions, or fragments thereof, and a heterologous peptide is high for the reasons of record. In addition, the instant specification provides detailed and extensive teachings on how to practice the claimed methods of making I-L-P' molecules and, further, provides working examples wherein the claimed methods were used to prepare I-L-P' molecules. Moreover, as in *In re Wands*, Applicants carry out the entire claimed process for making I-L-P' molecules and successfully produce molecules with the desired biological activity that fall within the scope of the claims.

Therefore, based on the detailed and extensive teachings in the specification, the working examples, and the knowledge available to one of skill in the art, the ordinary skilled artisan would be able to make and use the claimed invention using only routine experimentation. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

Rejection of Claims 74-76 Under 35 U.S.C. 112, First Paragraph

The Examiner has also rejected claims 74-76 under 35 U.S.C. 112, first paragraph as, "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Specifically, the Examiner states

> Applicant has only disclosed a desired outcome and not has sufficiently described the desired therapeutic agent. MPEP §2145 clearly states that attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection (MPEP § 2129 and §2144.03). Furthermore, the arguments of counsel cannot take the place of evidence in the record. In the instant case the Applicant is asserting possession of therapeutic agents represented by the formula I-L-P' while no data, information, or teaching supports possession of any therapeutic agents

represented by the formula I-L-P' in the instant Specification {see *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness.") and MPEP § 716.01(c)}.

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. The instant claims are most analogous to *University of Rochester v. G.D. Searle & Co.*, 68 USPQ2d 1424 (DC WNY 2003) and *University of Rochester v. G.D. Searle & Co. et al* CAFC [(03-1304) 13 February 2004] wherein a claim consisted of a "reach-through-claim" where the desired properties of the product were known but the product was not disclosed. In the instant application, claim 74 is a "reach-through-claim" where therapeutic agents represented by the formula I-L-P' have known desired properties but the product itself is not has not been disclosed.

Applicants respectfully traverse this rejection for the reasons of record. However, in the interest of expediting prosecution, and in no way acquiescing to the Examiner's rejection, Applicants have amended the claims such that they are now directed to methods of preparing therapeutic agents comprising the formula I-L-P', wherein I is an immunoglobulin heavy chain constant region or fragment thereof that retains the ability to bind an Fc receptor; L is a linker group or a direct bond and P' is ***a peptide capable of binding to a β-amyloid protein***.

Contrary to the Examiner's assertions, Applicants describe the claimed invention in sufficient detail such that one of skill in the art would understand that Applicants were in possession of the claimed invention at the time of filing the instant application. Specifically, each of the components of the compound I-L-P' has a definite art-recognized structure. In addition, each of these components is specifically defined in the specification. For example, I is defined, at page 7, lines 13-22, to mean the constant region of any immunoglobulin heavy chain, *e.g.*, γ_1, γ_2, γ_3, γ_4, μ, α_1, α_2, δ, or ε heavy chain, or a fragment thereof. As submitted on the record, the Written Description Guidelines issued by the U.S. Patent and Trademark Office explicitly acknowledge that antibodies have a well know structure. 66 Fed. Reg.1099. L is defined, at page 8, line 25 through page 9, line 3, to mean a direct bond or agent that can link the immunoglobulin heavy chain constant region to a peptide capable of binding a target molecule. P' is defined at page 37, lines 9-12 to mean a peptide capable of binding a target protein.

Peptides and linking agents are known to have a particular structure. Therefore, the claimed therapeutic agent is defined in terms of a class of molecules that possess both a particular structure and function.

As amended, component P' is a peptide capable of binding to a β-amyloid protein. The specification provides extensive description of the structure and function of P', for example, beginning at page 13, line 30 and ending at page 23, line 16 of the specification. Specifically, Applicants teach that P' is any peptide capable of binding to a β-amyloid protein and can be designed based on the amino acid sequence of β-AP, *e.g.*, designed based on the Aβ aggregation core domain (see for example, page 14, lines 13-15 of the specification). Applicants further provide a number of specific peptides that may be used as the component P', *e.g.*, $A\beta_{16-30}$, $A\beta_{17-20}$, $A\beta_{17-21}$, $A\beta_{16-25}$, $A\beta_{1-25}$, $A\beta_{1-40}$, and $A\beta_{1-42}$ Moreover, Applicants provide a list of peptides containing D amino acid isomers that are designed based on the Aβ aggregation core domain (see, for example, the 21 peptides set forth on page 19, lines 1-11 of the specification).

In *The Regents of the University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), one of the issues addressed by the Court of Appeals for the Federal Circuit was the sufficiency of a disclosure in meeting the written description requirement of 35 U.S.C. §112, first paragraph, for claims to a genus of molecules, *i.e.*, cDNAs. The Court stated that:

> [a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

Similarly, the instant specification discloses a representative number of I-L-P' compounds that fall within the scope of the claimed genus and defines them by structure. Accordingly, as set forth in *The Regents of the University of California* the genus of I-L-P' compounds, wherein P' is a peptide capable of binding to a β-amyloid protein meet the written description requirement of section 112, first paragraph.

The Examiner analogizes the present application to the application in *University of Rochester v. G. D. Searle & Co.*, 358 F.3d 916 (CAFC 2004). However, in the *University of Rochester v. G. D. Searle & Co* case, no compounds that would perform the claimed method were disclosed, nor was any evidence presented that such compounds were known. *Id* at *927*. In

contrast, the present specification describes several compounds that fall within the claimed genus, where P' is a peptide capable of binding to a β-amyloid protein.

In view of all of the foregoing, it is respectfully submitted that the instant specification satisfies the written description requirement of 35 U.S.C. § 112, first paragraph for the claimed invention. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

SUMMARY

If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Dated: February 24, 2005

Respectfully submitted,

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